REMARKS

After entry of the present amendments, claims 1 to 7 will remain pending. Claim 1 is presently amended to clarify the structure of the *o*-xylylene group and its point of attachment to the parent molecule. The amendment is supported in the application as filed by the parenthetical at page 3, first full paragraph, which indicates that the *ortho*-xylylene group has the formula *o*-$C_6H_4(CH_2)_2$. As one of ordinary skill in the art would understand, if the point of attachment of this group were other than where indicated in the amendment (for example, as suggested as an alternative at page 3 of the Office Action), the terminal groups would have been CH_3 instead of CH_2. No new matter is added.

Additionally, the specification has been amended to include a Cross-Reference to Related Applications section. The new paragraph makes explicit that the application represents entry into the U.S. national stage of PCT/GB03/00908 filed March 4, 2003, which in turn claims priority of GB 0205527.5, filed March 8, 2002. This is the same priority claim which is set forth on the Application Data Sheet and in the Oath/Declaration already of record in this case. A certified copy of the priority application has also been submitted previously, and priority of the 2002 foreign application has previously been recognized on both the Bib Data Sheet and filing receipt associated with this application. Since the claim to priority was properly made both on filing of the PCT application and upon entry into the U.S. national stage, Applicant respectfully submits that the priority claim was timely made.

Claims 8, 9 and 12 are canceled herein, without prejudice to pursuit of same in one or more continuing applications.

Rejection Under 35 U.S.C. § 102(f)

The pending claims stand rejected under 102(f) over the Griesbacher reference of record. Applicants respectfully submit that this reference is not prior art to the instant application, which has an effective filing date of March 8, 2002. Indeed, as clearly indicated in the Griesbacher reference (last page), it was not received by the Journal in question (much less published) until after the effective date of the instant application. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C § 112, first paragraph

The Office Action dated January 15, 2009 maintained the prior rejection of claims 8 to 12 as allegedly not enabled. This rejection has been rendered moot by the cancellation (without prejudice) of these claims.

Rejection Under 35 U.S.C § 103

The pending claims stand rejected as allegedly obvious over McIver et al, WO 93/08211, in view of Garret (of record) and Peak (of record). Applicants respectfully traverse.

As an initial matter, it is stated in the Office Action dated July 17, 2008, when this rejection was originally made, that "McIver et al. '211 disclosed structurally similar compounds for the instant activity in treating pain and inflammation", with the particular species shown in CA119:226431 being identified as the most relevant. However, McIver does NOT teach that the species in question has any activity at all! Indeed, the species cited in the Office Action is described in McIver et al. '211 as being an *intermediate*, that may be used to *prepare* compounds having usefulness for treating pain and inflammation (*see* McIver '211 at pages 14-15). Notably, the cited species is NOT within the scope of compounds said to be useful for treating pain and inflammation (*see e.g.*, McIver '211 at pages 2-3). Accordingly, one seeking to identify kallikrein inhibitors would not have any motivation to modify the species described in McIver, as suggested in the Office Action.

Further, as noted in Applicant's prior response, both the 1,3 connectivity of the piperidinyl group and the 2-oxo substitution of the piperidyl moiety are *required* for preparation of the arginine moiety that is present in the final, active compounds described in the McIver reference. If the species described in the McIver reference were modified to remove the oxo substitution and to utilize a 1,4 (instead of 1,3) connection of the piperidinyl moiety, the compound would no longer be suitable for reaction to "open" the ring and produce the arginine moiety present in the final compounds. Applicant respectfully submits that there can be no *prima facie* case of obviousness if the proposed modification to prior art would render the art "unsatisfactory" for its intended purpose. *See* MPEP § 2143.01.V.

Combination with either of the Peake or Garrett references fails to overcome the deficiencies of McIver '211. Peake, for example, is directed to compounds that are inhibitors of complement breakdown, not kallikrein inhibitors, so it also fails to provide the requisite motivation to modify the compounds described in the McIver reference. In addition, while the reference does describe a compound having a piperidinyl moiety that does not bear the oxo substitution, it is not connected in the molecule in a 1,4 configuration, as in the compounds of the present invention. Thus, there is nothing in the reference that would teach or suggest that "cyclic arginine (piperidine) or arginine aledhydes (oxo piperidine) are interchangeable units" as the Office asserts (*see* Office Action dated July 17, 2008, page5). Similarly, the Garrett reference describes only oxo-substituted piperidinyl moieties that have the 1,3 configuration, which may then be "opened" to give active compounds that are not within the scope of the instant claims. This reference, too, even if combined with McIver and/or Peake, fails to overcome the foregoing deficiencies.

Accordingly, Applicant respectfully submits that the Office Action fails to establish the *prima facie* obviousness of the pending claims. Withdrawal of the rejection under Section 103 is respectfully requested.

Conclusion

Applicants believe that the foregoing constitutes a complete and full response to the official action of record. Accordingly, a Notice of Allowance of pending claims 1 to 8 is requested.

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